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THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: Tomoaki HOSHINO et al. JUL -6 PM 1:21 Group Art Unit: 1644 PM 1:21

Serial No.: 10/695,875

Examiner: Yunsoo Kim

Filed: October 30, 2003

Confirmation No.: 6666

For: PREVENTIVE OR THERAPEUTIC AGENTS FOR DERMATITIS OR
ALOPECIA, EVALUATION METHOD OF THE AGENTS, AND
TRANSGENIC MOUSE

Attorney Docket Number: 032079
Customer Number: 38834

REQUEST FOR REFUND

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Date: June 30, 2005

Sir:


The undersigned respectfully requests a refund of 50% of the fees paid in the subject application on June 9, 2005.

The fees for the additional claims fee of \$150.00 and the extension fee of \$120.00 paid on June 9, 2005 were those for a large entity. The application, however, is entitled to the reduced fees provided for small entities under 37 CFR 1.16.

It is respectfully requested that the 50% excess of the fees paid (\$75.00 and \$60.00, respectively, i.e., a total of \$135.00) be credited to Deposit Account 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP


Nicolas E. Seckel
Attorney for Applicant
Registration No. 44,373

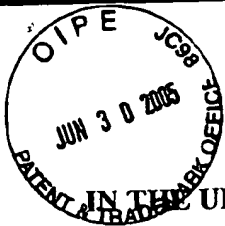
1250 Connecticut Avenue, NW
Suite 700
Washington, D.C. 20036
Tel: (202) 822-1100
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Encls: Copy of Extension of Time; Amendment Transmittal w/Amendment Fd. 06/09/2005
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2005 JUL -6 PM 1:21

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PETITION FOR EXTENSION OF TIME

COPY

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Date: June 9, 2005

Sir:

Applicants petition the Commissioner for Patents to extend the time for response to the Office Action dated February 10, 2005 for one month(s) from May 10, 2005 to June 10, 2005.

Attached please find a check in the amount of **\$270.00** to cover the cost of the extension (**\$120.00**) and additional claims fee (**\$150.00**). If any additional fees are due in connection with this paper, please charge our Deposit Account No. 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP

Nicolas E. Seckel

Nicolas E. Seckel

Attorney for Applicants

Registration No. 44,373

Telephone: (202) 822-1100

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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AMENDMENT TRANSMITTAL

COPY

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Date: June 9, 2005

Sir:

Transmitted herewith is an Amendment in the above-identified application. The fee has been calculated as shown below.

| | CLAIMS REMAINING AFTER AMENDMENT | | HIGHEST NUMBER PREVIOUSLY PAID FOR | PRESENT EXTRA |
|-----------------------------------------------------------------|-------------------------------------------|-------|---------------------------------------------|------------------|
| Total (37 CFR 1.16(c)) | 23 | Minus | 20 | = 3 |
| Independent (37 CFR 1.16(b)) | 1 | Minus | 4 | = 0 |
| FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(d)) | | | | |

| SMALL ENTITY | | OR | OTHER THAN SMALL ENTITY | |
|--------------------|------------------------|----|----------------------------|------------------------|
| RATE | ADDI- TIONAL FEE | | RATE | ADDI- TIONAL FEE |
| X \$25 | | OR | X\$50 | 150.00 |
| X \$100 | | OR | X\$200 | .00 |
| + \$180 | | OR | + \$360 | .00 |
| TOTAL ADD'L FEE | | | TOTAL ADD'L FEE | 150.00 |

☒ Enclosed please find our check in the amount of **\$270.00** for the additional claims fee (**\$150.00**) and extension fee (**\$120.00**) in connection with this Amendment.

☒ The Commissioner is hereby authorized to charge payment for any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP

Nicolas E. Seckel

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UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Tomoaki HOSHINO et al.

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Serial Number: 10/695,875

Group Art Unit: 1644

Filed: October 30, 2003

Examiner: KIM, YUNSOO

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EVALUATION METHOD OF THE AGENTS, AND TRANSGENIC MOUSE

COPY

Atty. Docket No.: 032079

Customer No.: 38834

AMENDMENT UNDER 37 C.F.R. 1.111

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir:

June 9, 2005

In response to the Office Action dated February 10, 2005, Applicants respectfully request that the application be amended as follows, and that the rejection of record be reconsidered in view of the following remarks.

Amendments to the Claims are reflected in the listing of claims that begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

An article by Kawano et al., Science Vol. 278 (1997), pp. 1626-1629, is submitted with this paper.

Also, a petition for a one-month extension of the time period for response is submitted with this paper.

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-11. (Canceled)

12. (New): A method of preventing or treating dermatitis and/or alopecia, comprising administering to a patient an effective amount of a composition comprising at least one antibody against NK cells selected from the group consisting of antibodies identifying an NK1.1 antigen, antibodies identifying an asialo GM1 antigen, and anti-Ly 49D antibodies.

13. (New): The method of claim 12, wherein the antibody is an antibody that suppresses NK cells.

14. (New): The method of claim 13, wherein the antibody is an antibody identifying an NK1.1 antigen.

15. (New): The method of claim 14, wherein the antibody is an antibody identifying human NK1.1 antigen.

16. (New): The method of claim 13, wherein the antibody is an antibody identifying an asialo GM1 antigen.

17. (New): The method of claim 13, wherein the at least one antibody is selected from the group consisting of antibodies identifying an NK1.1 antigen and antibodies identifying an asialo GM1 antigen.

18. (New): The method of claim 12, wherein the antibody is an antibody against an antigen that activates NK cells.

19. (New): The method of claim 18, wherein the antibody is anti-Ly 49D antibody.
20. (New): The method of claim 12, wherein the composition is administered topically.
21. (New): The method of claim 20, wherein the composition is administered directly onto the skin.
22. (New): The method of claim 20, wherein the composition is administered subcutaneously.
23. (New): The method of claim 20, wherein the composition is administered intramuscularly.
24. (New): The method of claim 12, wherein the composition is administered systemically.
25. (New): The method of claim 24, wherein the composition is administered by injection.
26. (New): The method of claim 24, wherein the composition is administered intravenously.
27. (New): The method of claim 12, which is a method of preventing or treating dermatitis.
28. (New): The method of claim 12, which is a method of preventing or treating alopecia.
29. (New): The method of claim 28, wherein the alopecia is caused by dermatitis.
30. (New): The method of claim 12, which is a method of preventing or treating psoriasis.
31. (New): The method of claim 12, which is a method of preventing or treating autoimmune dermatitis.
32. (New): The method of claim 12, which is a method of preventing or treating allergic dermatitis.
33. (New): The method of claim 12, which is a method of preventing or treating atopic dermatitis.

Serial Number: 10/695,875

Group Art Unit: 1644

34. (New): The method of claim 12, which is a method of preventing or treating dermal disorders derived from overexpression of IL-18.

REMARKS

As a preliminary, Applicants and Applicants' representative thank the Examiner and her Supervisor for the personal interview held on May 23, 2005.

By the present amendment, claims 7-9 have been canceled and new claims 12-34 have been added. Support for new claims 12-34 is found in original claims 7-9 and page 11, lines 3-9 (claims 13-14 and 16-19), page 12, line 3 (claim 15), page 12, lines 5-13 (claims 20-26), page 21, lines 15-19 (claims 27-28, 30 and 32), page 17, line 20 (claim 29) and page 1, line 13 (claims 31 and 33).

Consideration of new claims 12-34 is respectfully requested. It is submitted that the redrafting of the species of claims 7-9 into method claims 12-34 does not constitute a change of elected species, as the agent remains within the same species. In any case, it is submitted that the change from agent to method claims does not impose a substantial burden on the Examiner, as the substance of new claims 12-34 remains within the same species, even though the claims are now in method format. Accordingly, further examination of the method claims is respectfully requested.

Further, it is submitted that the subject matter of claims 12-34 corresponds to the species of Group I, anti-NK cell agents, which was elected in the response filed December 2, 2004 to the restriction requirement of November 17, 2004. Specifically, claim 12 recites a composition comprising at least one antibody against NK cells, wherein the at least one antibody is selected from the group consisting of antibodies identifying an NK1.1 antigen, antibodies identifying an asialo GM1 antigen, and anti-Ly 49D antibodies. Each of the at least one antibody against NK cells of claim 12 is within the elected species of Group I, i.e., anti-NK cell agents. In particular, antibodies identifying an NK1.1 antigen and antibodies identifying an asialo GM1 antigen are

antibodies that suppress NK cells, and anti-Ly 49D antibodies are antibodies that identify an antigen that activates NK cells, i.e., they are anti-NK cell agents, as discussed on page 11, lines 3-9 of the specification.

In view of the above, it is submitted that the subject matter of claims 12-34 should be fully examined.

In the Office Action, the claim for priority is acknowledged, but certified copies of the priority documents are requested.

It is submitted that the certified copies of the priority documents have already been filed as attachments to the claim for priority on October 30, 2003.

Next, in the Office Action, claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, as not enabled. It is alleged in the Office Action that that the specification is enabling only for "an anti-NK1.1 antibody agent for treating dermatitis by suppressing a cell having an NK 1.1 antigen."

Reconsideration and withdrawal of the rejection is respectfully requested. Present claim 12 recites at least one antibody against NK cells selected from the group consisting of antibodies identifying an NK1.1 antigen, antibodies identifying an asialo GM1 antigen, and anti-Ly 49D antibodies. It is submitted that the present specification is enabling, not only for administration of antibodies that suppress NK cells (see Examples 2 and 3 at pages 15-17), but also for administration of antibodies against NK cells. In particular, the present inventors have disclosed and illustrated in the specification the effect of administration of antibodies identifying an antigen that activates NK cells, based on the exemplification of anti-Ly 49D antibody (see Example 5 at pages 19-20).

Further, it is submitted that the teachings of the present specification are sufficient to

enable, not only treatment, but also prevention of dermatitis and/or alopecia. Namely, the present inventors have demonstrated that administration of the agent against NK cells to mice that have been genetically modified to trigger dermatitis, starting at birth, prevents (i.e., "suppresses") any occurrence of dermatitis, whereas dermatitis is triggered in the comparative mice (see, e.g., Example 2 at page 15, lines 23-24, Example 3 at page 16, lines 25-26, and Example 5 at page 19, lines 26-27). These teachings regarding prevention and treatment are consistent with the knowledge of the processes at the source of the onset of dermatitis, as explained for example on pages 7-8 of the specification, and would be understood by the person of ordinary skill in the art as establishing effectiveness for prevention as well as treatment.

In summary, the preventive and treating effects of each of the at least one antibody against NK cells recited in present claim 12 is sufficiently disclosed, illustrated, and exemplified in the present specification, so that the present claims are enabled.

In view of the above, it is submitted that the lack of enablement rejection should be withdrawn.

Next, in the Office Action, claims 7-9 are rejected under 35 U.S.C. 102(b) as anticipated by WO 00/02923 ("Nickoloff"). It is alleged in the Office Action that Nickoloff teaches the use of antibody for CD161 antigen of NK-T cells to prevent or treat psoriasis.

Reconsideration and withdrawal of the rejection is respectfully requested. It is submitted that Nickoloff has failed to disclose an antibody against CD161 of NKT cells, because the CD1d proposed by Nickoloff is known to bind to the TCR receptor of NKT cells, and not to CD161.

In support of the above explanation, an article by Kawano et al., CD1d-Restricted and TCR-Mediated Activation of V α 14 NKT Cells by Glycosylceramides, Science Vol. 278 (1997),

pp. 1626-1629), is submitted with this paper. The Kawano article explains the known relationship between CD1d and TCR receptor (see Kawano at page 1627, right col.). This article confirms that the purported relationship between CD161 and CD1d indicated on the last line of Table II on page 12 and on Fig. 1 of Nickoloff is erroneous. In other words, Nickoloff has not shown an antibody against CD161, but has only demonstrated in its Example 3 on pages 44-45 in vitro inhibition by CD1d of peripheral cells (presumably a majority of NKT cells) isolated from a psoriatic patient.

Given these serious deficiencies of Nickoloff, a person of the art would not rely on Nickoloff as a basis for researching improvements or modifications of the method of Nickoloff. In addition, even if, arguendo, a person of ordinary skill in the art had been motivated to further study the method of Nickoloff, that person would have been aware that (i) Nickoloff has not disclosed whether a CD161 antibody would be effective against psoriasis, and (ii) TCR receptors are present on NKT cells and not NK cells. Correspondingly, that person would find no suggestion or motivation in Nickoloff to use a CD161 antibody, or other various antibodies against NK cells, in order to prevent or treat dermatitis and/or alopecia, because Nickoloff does not provide any guidance or reasonable expectation of success as to such endeavors.

In contrast, the present inventors have demonstrated that antibodies against NK cells, i.e., the antibodies as recited in present claim 12, can be used effectively to prevent or treat dermatitis and/or alopecia. In particular, the present inventors have shown that antibodies identifying an NK1.1 antigen, antibodies identifying an asialo GM1 antigen, and anti-Ly 49D antibodies can prevent or treat dermatitis and/or alopecia. The effect of these antibodies targeting NK cells is considerably more effective than the effect of targeting NKT cells as in Nickoloff. For example, Example 3 of the present specification shows that the antibody against asialo GM1 antigen, which

is present in NK cells but not NKT cells, prevented the onset of dermatitis, whereas Comparative Examples 1 and 2 (pages 16-17 and Figs. 8-9) show that antibodies against CD4 and CD8 which are present in NKT cells and not NK cells, could not prevent dermatitis. The effects of antibodies identifying an NK1.1 antigen and anti-Ly 49D antibodies to prevent or treat dermatitis are also completely unexpected from Nickoloff.

In summary, the presently claimed method of preventing or treating dermatitis and/or alopecia and its advantages are not taught or suggested in Nickoloff. Therefore, the present claims are not obvious over Nickoloff.

In view of the above, it is submitted that the rejection should be withdrawn.

In conclusion, the invention as presently claimed is patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

Serial Number: 10/695,875

Group Art Unit: 1644

In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP



Nicolas E. Seckel
Attorney for Applicants
Reg. No. 44,373

Atty. Docket No.: 032079

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U.S. Patent Application
Serial No.: 10/695,875
Applicant: Tomoaki HOSHINO et al.

Docket No: 032079
Filed: October 30, 2003

Papers filed herewith on: June 9, 2005

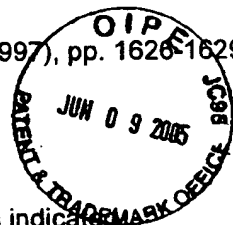
Fees: \$270.00 = \$120.00 (1st EOT) + \$150.00 (extra claims)

Petition for Extension of Time

Amendment Transmittal

Amendment under 37 C.F.R. 1.111 w/

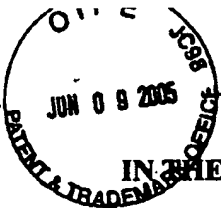
Article by Kawano et al., Science Vol. 278 (1997), pp. 1626-1629



COMMISSIONER OF PATENTS

Receipt is hereby acknowledged of the papers filed as indicated
in connection with the above-identified case.

NES/ya



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: **Tomoaki HOSHINO et al.**

Group Art Unit: 1644

Serial No.: 10/695,875

Examiner: Yunsoo Kim

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06/10/2005 SDENB081 00000030 10695875

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Adjustment date: 08/08/2005 SDIRETA1
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NES/ya

08/08/2005 SDIRETA1 00000059 10695875

01 FC:2251 60.00 OP



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Adjustment date: 08/08/2005 SDIRETA1

06/10/2005 SDENB081 00000030 10695875

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